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ARTICLE TYPE

## Titanium pyridonates for the homo- and copolymerization of *rac*-lactide and $\epsilon$ -caprolactone

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A series of titanium pyridonate complexes have been synthesized under very mild reaction conditions from a common precursor,  $\text{Ti}(\text{NMe}_2)_4$ . These complexes have been explored as initiators for the ring-opening polymerization of *rac*-lactide and  $\epsilon$ -caprolactone and have proven to be competitive with leading titanium initiators. Furthermore, these complexes have been shown to be competent initiators for the synthesis of copolymers (CL-LA block copolymers and random copolymers). Metal complex reactivity trends in both homo- and copolymerization show that poly(lactic acid) is most susceptible to chain scission and transesterification.

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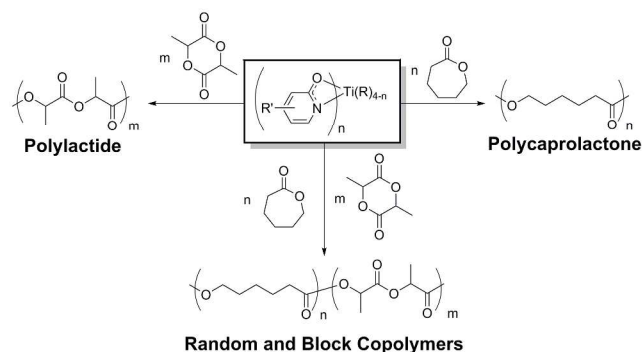
## ARTICLE TYPE

## Introduction

The field of biodegradable polymer research has experienced a marked increase in interest over the past years.<sup>1</sup> Investigations into the polymerization of lactide (LA) and  $\epsilon$ -caprolactone (CL), to generate poly(lactic acid) (PLA) and poly( $\epsilon$ -caprolactone) (PCL) respectively, are largely driven by their potential applicability as substitutes for commodity plastics derived from polyolefins. The most commonly utilized mechanism to conduct well-controlled polymerizations is the ring-opening of cyclic esters by an initiator, often a metal complex.<sup>2, 3</sup> These polymers have practical merit in many traditional applications as well as specialized utility in fields such as biomedical materials as oral implants, sutures, and microspheres for drug delivery purposes.<sup>4, 5</sup>

Aside from the homopolymerization of lactide and  $\epsilon$ -caprolactone, these monomers can be used to prepare copolymers which, depending upon their composition, allows for a range of physical and mechanical properties.<sup>6–11</sup> Copolymerization has emerged as an attractive strategy for modulating the brittle mechanical properties of PLA that limit its broader application. An important synthetic challenge is the ability to form random copolymers that possess equal incorporation of monomers in the polymer backbone. This can be challenging due to the differences in monomer reactivity and relative polymerization rates.<sup>7</sup> Some examples of random co-polymer synthesis have been reported, including our initially communicated titanium pyridonate system.<sup>12–15</sup>

The investigation of titanium complexes as initiators<sup>12–29</sup> for the ring-opening polymerization of cyclic esters has been largely driven by the minimal cost, high abundance, and low toxicity<sup>30</sup> of the source metal. While they are as yet less competitive than the leading initiator systems, these practical advantages have motivated vigorous research interest into a variety of ligand scaffolds in pursuit of achieving high molecular weight polymers with control of dispersity, co-monomer incorporation and tacticity.<sup>31</sup> Selected titanium examples include species ligated with tetradentate amino-phenolates,<sup>32</sup> salen ligands,<sup>33</sup> catecholates,<sup>34</sup> aminodiols,<sup>12</sup> thioetherphenolates,<sup>13</sup> sulfur or tellurium bridged bimetallic species,<sup>28</sup> and sulfonamide supported complexes.<sup>21</sup> Typically, these complexes range from tetra- to hexa-coordinate species with bulky ancillary ligand(s) to vary the steric and electronic environment about the metal center. In addition, they also possess one or more 'reactive' ligands (alkoxide, aryloxide, and halogen initiating ligands<sup>23, 35, 36</sup>) that function as the nucleophilic ligand for polymerization initiation. Most commonly, initiators with two reactive ligands are proposed to propagate two polymer chains for each metal center.<sup>12, 16, 20</sup> However, in some cases it has been suggested that only one of the two reactive ligands initiates if the metal center is sterically crowded.<sup>16</sup>



**Figure 1** Polymers accessible *via* ring-opening polymerization using titanium pyridonate initiators

Previously, we have reported the ability of a unique class of titanium *N,O*-chelated complexes to afford poly(lactic acid) as well as random copolymers of poly(lactic acid)-*co*-caprolactone with close to equal monomer incorporation.<sup>15</sup> Analysis of these copolymers suggested extensive transesterification, which has been shown to contribute to the randomization of monomers along the polymer chain.<sup>15</sup> Herein we present a full analysis of these titanium pyridonate complexes, including an evaluation of structure and bonding. The influence of variable pyridonate substitution was explored in the synthesis of poly(lactic acid), poly( $\epsilon$ -caprolactone), random co-polymers and block copolymers. A comparison of initiating reactive nucleophilic ligands has also been conducted. The preparation of both bis- and tris-pyridonate substituted complexes has been completed to probe the assumption that two polymer chains result from each metal center. The comparison of reactivity trends in random copolymer formation, with simultaneous monomer addition, and in block copolymer synthesis, with sequential addition of  $\epsilon$ -caprolactone followed by lactide, is reported. The versatility of these complexes in cyclic ester polymerization is detailed within.

## Experimental

**Reagents** All reagents were purchased from commercial sources. Proligands were purified by sublimation then stored and manipulated in a nitrogen filled glovebox. Alcohols were stirred over 3 Å molecular sieves for 18 h then distilled and degassed using three freeze-pump-thaw cycles. All synthetic steps were carried out in a nitrogen filled glovebox. *rac*-Lactide was sublimed once then stored in a freezer (-30 °C) in a nitrogen-filled glovebox.  $\epsilon$ -Caprolactone was stirred over CaH<sub>2</sub> for a minimum of 2 h, separated by distillation, then manipulated using standard Schlenk techniques.

**Analysis** Polymer  $M_n$ ,  $M_w$  and dispersity ( $\bar{D}$ ) were obtained using triple detection gel permeation chromatography (GPC) using a Waters liquid chromatograph equipped with an Agilent 1200 series isocratic pump and autosampler, Phenomenex

Phenogel 5  $\mu\text{m}$  narrow bore columns, Wyatt OptilabEx differential refractometer, Wyatt tristar miniDAWN (laser light scattering detector) and a Wyatt ViscoStar viscometer. A flow rate of 0.5 ml·min<sup>-1</sup> was used and samples were dissolved in THF ( $\sim 2 \text{ mg}\cdot\text{ml}^{-1}$ ). The measurements were carried out at a laser wavelength of 690 nm, at 25 °C. The data was analyzed using the Astra® processing program provided by Wyatt Technology Corp. All dn/dc values were calculated from 100% mass recovery methods using the aforementioned GPC software. The dn/dc values for homopolymers poly(lactide) and poly(caprolactone) typically ranged from 0.041-0.043 and 0.071-0.074, respectively, and copolymers gave dn/dc values typically ranging from 0.050 to 0.065. <sup>1</sup>H NMR spectra were collected using a Bruker Avance instrument operating at 300, 400, or 600 MHz. Abbreviations for NMR assignments are as follows: s = singlet; d = doublet; dd = doublet of doublets; t = triplet; q = quartet; m = multiplet; br = broad; appt = apparent. Random copolymer sequence lengths were calculated from <sup>13</sup>C NMR spectroscopy at 273 K using the Bruker Avance 400 or 600 instrument.

**General procedure for the synthesis of bis(pyridonate)-titanium-bis(dimethylamido) complexes.** In a nitrogen filled glovebox, a Teflon capped vial was charged with Ti(NMe<sub>2</sub>)<sub>4</sub> (yellow liquid, 224.2 g·mol<sup>-1</sup>) in 2-3 mL of benzene. Two equivalents of proligand (6- or 3-methyl pyridone, white solid, 109 g·mol<sup>-1</sup>) were added and a colour change to deep red was observed instantly. To ensure completion the solution was stirred at room temperature for 1 h. The solvent was then removed in *vacuo*. The resulting red residue was recrystallized using a minimum of benzene ( $\sim 1 \text{ mL}$ ) with 5-10 drops of hexanes and left to crystallize at -35 °C. The supernatant was then removed to afford the complex as a red crystalline solid. The complex was washed with a small amount of cold hexanes and dried in *vacuo*.

**1a** Red solid (90% yield). <sup>1</sup>H NMR (300 MHz; 298 K; *d*<sub>6</sub>-benzene)  $\delta$  6.92 (dd, <sup>3</sup>*J*<sub>H-H</sub> = 8.3 Hz, <sup>3</sup>*J*<sub>H-H</sub> = 7.3 Hz, 2H), 6.28 (d, <sup>3</sup>*J*<sub>H-H</sub> = 8.3 Hz, 2H), 5.90 (d, <sup>3</sup>*J*<sub>H-H</sub> = 7.3 Hz, 2H), 3.56 (s, 12H), 2.10 (s, 6H). <sup>13</sup>C NMR (100 MHz; 298 K; *d*<sub>6</sub>-benzene)  $\delta$  172.4, 154.1, 140.9, 112.4, 106.5, 47.0, 21.7; Anal. calcd. for C<sub>16</sub>H<sub>24</sub>N<sub>4</sub>O<sub>2</sub>Ti: C, 54.6; H, 6.9; N, 15.9. Found: C, 54.7; H, 6.8; N, 15.8.

#### Crystal structure determination of complex 1a

**Crystal data.** <sup>‡</sup> C<sub>16</sub>H<sub>24</sub>N<sub>4</sub>O<sub>2</sub>Ti, *M* = 352.29, triclinic, *a* = 8.890(6), *b* = 9.373(6), *c* = 12.326(8) Å, *U* = 1027.3(5) Å<sup>3</sup>, *T* = 100 K, space group P-1, *Z* = 2, 18600 reflections measured, 5115 unique (*R*<sub>int</sub> = 0.0702) which were used in all calculations. The final *wR*(*F*<sub>2</sub>) was 0.1473 (all data).

**2a** Red solid, (95% yield). <sup>1</sup>H NMR (300 MHz; 298 K; *d*<sub>6</sub>-benzene)  $\delta$  7.43 (d, <sup>3</sup>*J*<sub>H-H</sub> = 5.4 Hz, 2H), 6.86 (d, <sup>3</sup>*J*<sub>H-H</sub> = 7.1 Hz, 2H), 6.03 (dd, <sup>3</sup>*J*<sub>H-H</sub> = 7.1, <sup>3</sup>*J*<sub>H-H</sub> = 5.4 Hz, 2H), 3.55 (s, 12H), 2.16 (s, 6H). <sup>13</sup>C NMR (150 MHz; 298 K; *d*<sub>6</sub>-benzene)  $\delta$  171.6, 140.5, 140.0, 128.9, 119.3, 112.7, 46.8, 15.4; Anal. calcd. for C<sub>16</sub>H<sub>24</sub>N<sub>4</sub>O<sub>2</sub>Ti: C, 54.6; H, 6.9; N, 15.9. Found: C, 54.6; H, 6.6; N, 15.8.

**General procedure for the synthesis of bis-(pyridonate)-titanium-bis(alkoxide) complexes.** In a nitrogen filled glovebox, a Teflon capped vial was charged with bis-(pyridonate)-titanium-

bis(dimethylamido) in 1-2 ml of benzene. Stoichiometric equivalents of alcohol were added using a microsyringe. A colour change to clear yellow was observed instantly. The solution was stirred at room temperature for 1 h to ensure completion. The solvent was then removed in *vacuo* and the residue washed with 5 ml cold, dry hexanes. The complex was then dried in *vacuo*.

**1b** Pale yellow solid, (95% yield). <sup>1</sup>H NMR (300 MHz; 298 K; *d*<sub>6</sub>-benzene)  $\delta$  6.93 (dd, <sup>3</sup>*J*<sub>H-H</sub> = 7.3 Hz, <sup>3</sup>*J*<sub>H-H</sub> = 6.2 Hz, 2H), 6.25 (d, <sup>3</sup>*J*<sub>H-H</sub> = 6.2 Hz, 2H), 5.91 (d, <sup>3</sup>*J*<sub>H-H</sub> = 7.3 Hz, 2H), 4.51 (q, <sup>3</sup>*J*<sub>H-H</sub> = 7.0 Hz, 4H), 2.15 (s, 6H), 1.22 (t, <sup>3</sup>*J*<sub>H-H</sub> = 7.0 Hz, 6H). <sup>13</sup>C NMR (100 MHz; 298 K; *d*<sub>6</sub>-benzene)  $\delta$  173.4, 153.4, 141.7, 112.9, 106.4, 73.8, 21.5, 19.2; MS(EI) calcd. for C<sub>16</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub>Ti [M+]<sup>+</sup> 354.1059, found 354.1061; Anal. calcd. for C<sub>16</sub>H<sub>22</sub>N<sub>2</sub>O<sub>4</sub>Ti: C, 54.3; H, 6.3; N, 7.9. Found: C, 54.2; H, 6.4; N, 8.2.

#### Crystal structure determination of complex 1b

**Crystal data.** <sup>‡</sup> C<sub>16</sub>H<sub>21</sub>N<sub>2</sub>O<sub>4</sub>Ti, *M* = 353.25, orthorhombic, *a* = 56.949(5), *b* = 10.872(5), *c* = 11.211(5) Å, *U* = 6941(4) Å<sup>3</sup>, *T* = 100 K, space group Fdd2, *Z* = 4, 34715 reflections measured, 4952 unique (*R*<sub>int</sub> = 0.0702) which were used in all calculations. The final *wR*(*F*<sub>2</sub>) was 0.0882 (all data).

**1c** Pale yellow solid, (92% yield). <sup>1</sup>H NMR (300 MHz; 298 K; *d*<sub>6</sub>-benzene)  $\delta$  6.91 (app. s, 2H), 6.26 (d, <sup>3</sup>*J*<sub>H-H</sub> = 6.7 Hz, 2H), 5.90 (app. s, 2H), 4.86 (app. quintet, <sup>3</sup>*J*<sub>H-H</sub> = 5.9 Hz, 2H), 2.15 (s, 6H), 1.28 (d, <sup>3</sup>*J*<sub>H-H</sub> = 5.9 Hz, 12H). <sup>13</sup>C NMR (100 MHz; 298 K; *d*<sub>6</sub>-benzene)  $\delta$  173.4, 153.4, 141.6, 112.8, 106.2, 80.2, 26.0, 21.5; MS(EI) calcd. for C<sub>18</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>Ti [M+]<sup>+</sup> 382.1372, found 382.1374; Anal. calcd. for C<sub>18</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>Ti: C, 56.6; H, 6.9; N, 7.3. Found: C, 56.8; H, 6.9; N, 7.6.

#### Crystal structure determination of complex 1c

**Crystal data.** <sup>‡</sup> C<sub>18</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>Ti, *M* = 382.31, monoclinic, *a* = 11.5499(6), *b* = 13.1813(6), *c* = 26.740(1) Å, *U* = 3976(4) Å<sup>3</sup>, *T* = 100 K, space group p21/n, *Z* = 8, 63100 reflections measured, 9082 unique (*R*<sub>int</sub> = 0.0461) which were used in all calculations. The final *wR*(*F*<sub>2</sub>) was 0.0905 (all data).

**1d** Pale yellow oil, (94% yield). <sup>1</sup>H NMR (300 MHz; 298 K; *d*<sub>6</sub>-benzene)  $\delta$  7.37 (d, <sup>3</sup>*J*<sub>H-H</sub> = 7.3 Hz, 4H), 7.11 (dd, <sup>3</sup>*J*<sub>H-H</sub> = 7.7 Hz, <sup>3</sup>*J*<sub>H-H</sub> = 7.4 Hz, 4H), 7.03 (t, <sup>3</sup>*J*<sub>H-H</sub> = 7.3 Hz, 2H), 6.89 (dd, <sup>3</sup>*J*<sub>H-H</sub> = 8.0 Hz, <sup>3</sup>*J*<sub>H-H</sub> = 7.7 Hz, 2H), 6.24 (d, <sup>3</sup>*J*<sub>H-H</sub> = 8.0 Hz, 2H), 5.86 (d, <sup>3</sup>*J*<sub>H-H</sub> = 7.4 Hz, 2H), 5.56 (s, 4H), 2.05 (s, 6H). <sup>13</sup>C NMR (100 MHz; 298 K; *d*<sub>6</sub>-benzene)  $\delta$  172.7, 153.0, 141.4, 128.5, 127.0, 126.7, 112.7, 105.9, 79.3, 48.9, 21.0; MS(EI) calcd. for C<sub>26</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>Ti [M+]<sup>+</sup> 478.1372, found 478.1374.

**2b** Pale yellow solid, (90% yield). <sup>1</sup>H NMR (300 MHz; 298 K; *d*<sub>6</sub>-benzene)  $\delta$  7.46 (s, 2H), 6.88 (d, <sup>3</sup>*J*<sub>H-H</sub> = 6.6 Hz, 2H), 6.04 (appt t, <sup>3</sup>*J*<sub>H-H</sub> = 5.6 Hz, 2H), 4.89 (app. t, <sup>3</sup>*J*<sub>H-H</sub> = 6.1 Hz, 2H), 2.08 (s, 6H), 1.26 (d, <sup>3</sup>*J*<sub>H-H</sub> = 6.1 Hz, 12H). <sup>13</sup>C NMR (100 MHz; 298 K; *d*<sub>6</sub>-benzene)  $\delta$  171.2, 141.9, 139.7, 121.3, 112.8, 78.9, 26.2, 16.3; MS(EI) calcd. for C<sub>18</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>Ti [M+]<sup>+</sup> 382.1372, found 382.1372; Anal. calcd. for C<sub>18</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>Ti: C, 56.6; H, 6.9; N, 7.3. Found: C, 56.2; H, 6.6; N, 7.3.

**General procedure for the synthesis of the tris(pyridonate)-titanium(dimethylamido) complex.** In a nitrogen filled glovebox, a Teflon capped vial was charged with Ti(NMe<sub>2</sub>)<sub>4</sub> (yellow liquid, 224.2 g·mol<sup>-1</sup>) in 2-3 ml of benzene. One

equivalent of proligand (white solid,  $109 \text{ g}\cdot\text{mol}^{-1}$ ) was added and a colour change to red was observed instantly. To ensure reaction completion the solution was stirred at room temperature for 24 h. The solvent was then removed in *vacuo*. The residue was recrystallized using a minimum of toluene (1-2 mL). The supernatant was then removed to afford the complex as a red solid. The complex was washed with a small amount of cold hexanes then dried in *vacuo*.

**3a** Red-brown solid, (87% yield).  $^1\text{H}$  NMR (300 MHz; 298 K;  $d_6$ -benzene)  $\delta$  6.93 (dd,  $^3J_{\text{H-H}} = 8.1 \text{ Hz}$ ,  $^3J_{\text{H-H}} = 7.4 \text{ Hz}$ , 3H), 6.33 (d,  $^3J_{\text{H-H}} = 8.1 \text{ Hz}$ , 3H), 6.02 (d,  $^3J_{\text{H-H}} = 7.4 \text{ Hz}$ , 3H), 3.75 (s, 6H), 2.24 (s, 9H).  $^{13}\text{C}$  NMR (100 MHz; 298 K;  $d_6$ -benzene)  $\delta$  172.2, 155.1, 140.8, 113.6, 107.6, 49.4, 22.5; MS(EI) calcd. for  $\text{C}_{18}\text{H}_{18}\text{N}_3\text{O}_3\text{Ti}$  [M-(NMe<sub>2</sub>)] 372.0828, found 372.0827; Anal. calcd. for  $\text{C}_{20}\text{H}_{24}\text{N}_4\text{O}_3\text{Ti}$ : C, 57.7; H, 5.8; N, 13.5. Found: C, 57.5; H, 5.7; N, 13.6.

#### Crystal structure determination of complex 3a

**Crystal data.**  $\text{C}_{20}\text{H}_{24}\text{N}_4\text{O}_3\text{Ti}$ ,  $M = 416.33$ , monoclinic,  $a = 15.541(5)$ ,  $b = 15.777(5)$ ,  $c = 17.710(5) \text{ \AA}$ ,  $U = 3990(2) \text{ \AA}^3$ ,  $T = 100 \text{ K}$ , space group  $p2_1/c$ ,  $Z = 8$ , 47362 reflections measured, 11864 unique ( $R_{\text{int}} = 0.0351$ ) which were used in all calculations. The final  $wR(F_2)$  was 0.0587 (all data).

**General procedure for the synthesis of tris(pyridonate)-titanium(alkoxide) complex.** In a nitrogen filled glovebox, a Teflon capped vial was charged with tris(pyridonate)-titanium-(dimethylamido) precursor in 1-2 ml of benzene. A stoichiometric equivalent of alcohol was added using a microsyringe. A colour change to clear yellow was observed instantly. The solution was stirred at room temperature for 1 h to ensure completion of the reaction. The solvent was then removed in *vacuo* then the residue washed with 5 ml cold, dry hexanes. The hexane solution was then concentrated in *vacuo* to afford the pure complex.

**3b** Yellow solid, (90% yield).  $^1\text{H}$  NMR (300 MHz; 298 K;  $d_6$ -benzene)  $\delta$  6.94 (dd,  $^3J_{\text{H-H}} = 7.9 \text{ Hz}$ ,  $^3J_{\text{H-H}} = 7.7 \text{ Hz}$ , 3H), 6.40 & 6.25 (d,  $^3J_{\text{H-H}} = 6.5 \text{ Hz}$ , 3H, ratio 9:1), 6.03 & 5.92 (d,  $^3J_{\text{H-H}} = 6.5 \text{ Hz}$ , 3H, ratio 9:1), 4.86 & 4.74 (septet,  $^3J_{\text{H-H}} = 6.2 \text{ Hz}$ , 1H, ratio 7:25), 2.21 (s, 9H), 1.28 & 1.20 (d,  $^3J_{\text{H-H}} = 6.2 \text{ Hz}$ , 6H, ratio 7:25).  $^{13}\text{C}$  NMR (100 MHz; 298 K;  $d_6$ -benzene)  $\delta$  172.2, 154.4, 141.5, 140.9, 114.1, 112.8, 107.8, 106.3, 83.2, 80.3, 26.0, 25.5, 22.5, 21.6; MS(EI) calcd. for  $\text{C}_{21}\text{H}_{25}\text{N}_3\text{O}_4\text{Ti}$  [M+] 431.1325, found 431.1326; Anal. calcd. for  $\text{C}_{21}\text{H}_{25}\text{N}_3\text{O}_4\text{Ti}$ : C, 58.5; H, 5.8; N, 9.7. Found: C, 58.2; H, 5.8; N, 9.4.

#### Crystal structure determination of complex 3b

**Crystal data.**  $\text{C}_{21}\text{H}_{25}\text{N}_3\text{O}_4\text{Ti}$ ,  $M = 431.34$ , triclinic,  $a = 8.742(5)$ ,  $b = 8.895(5)$ ,  $c = 14.240(5) \text{ \AA}$ ,  $U = 1064.7(9) \text{ \AA}^3$ ,  $T = 100 \text{ K}$ , space group  $P-1$ ,  $Z = 2$ , 32693 reflections measured, 6294 unique ( $R_{\text{int}} = 0.0344$ ) which were used in all calculations. The final  $wR(F_2)$  was 0.1170 (all data).

#### General procedure for the homopolymerization of LA or CL.

In a nitrogen filled glovebox, a Kontes®-valve reaction tube was charged with a stirrer bar. The appropriate quantity of catalyst was added from a standard solution in toluene, the solvent was removed in *vacuo* before adding  $\epsilon$ -CL (clear, colourless liquid, 300 equivalents,  $0.396 \text{ g}$ ,  $114.14 \text{ g}\cdot\text{mol}^{-1}$ ) or *rac*-LA (clear, colourless solid, 300 equivalents,  $0.500 \text{ g}$ ,  $144.13 \text{ g}\cdot\text{mol}^{-1}$ ). PCL

synthesis was carried out at  $100 \text{ }^\circ\text{C}$  for 16 h. PLA synthesis was carried out at  $130 \text{ }^\circ\text{C}$  for 24 h. Either reaction was then quenched with 10 mL of dichloromethane and allowed to dissolve. The resulting viscous solution was precipitated directly into freezing cold methanol, filtered, and washed with small amounts of methanol. It was then dried under vacuum for a minimum of 8 hours to obtain the isolated polymer (white solid for PCL, off-white/light brown solid for PLA).

**Poly(lactic acid) (PLA)** (see SI)  $^1\text{H}$  NMR (300 MHz;  $\text{CDCl}_3$ )  $\delta$  5.24-5.11 (m,  $\text{C(O)CH(CH}_3\text{)}$ , 2H), 1.59-1.52 (br m,  $\text{C(O)CH(CH}_3\text{)}$  6H).

**Poly( $\epsilon$ -caprolactone) (PCL)** (see SI)  $^1\text{H}$  NMR (300 MHz;  $\text{CDCl}_3$ )  $\delta$  4.06 (br t,  $\text{CH}_2\text{CH}_2\text{OC(O)CH}_2\text{CH}_2\text{CH}_2$ , 2H) 2.31 (t,  $\text{CH}_2\text{CH}_2\text{OC(O)CH}_2\text{CH}_2\text{CH}_2$ , 2H), 1.67-1.32 (br m,  $\text{CH}_2\text{CH}_2\text{OC(O)CH}_2\text{CH}_2\text{CH}_2$ , 6H).

**General procedure for the random copolymerization of LA and CL.** In a nitrogen filled glovebox, a Kontes®-valve reaction tube was charged with a stirrer bar and the appropriate quantity of catalyst was added from a standard solution in toluene, and then the solvent was removed in *vacuo*. Random copolymerizations were carried out with simultaneous addition of CL (clear, colourless liquid, 300 equivalents,  $0.396 \text{ g}$ ,  $114.14 \text{ g}\cdot\text{mol}^{-1}$ ) and *rac*-LA (clear, colourless solid, 300 equivalents,  $0.500 \text{ g}$ ,  $144.13 \text{ g}\cdot\text{mol}^{-1}$ ) followed by heating at  $130 \text{ }^\circ\text{C}$  using a preheated oil bath for 24 h. The reaction was then worked-up as with the homopolymerizations to obtain the isolated polymer (brown, sticky solid).

**Poly(lactide-co-caprolactone) PLA-co-PCL** (see SI)  $^1\text{H}$  NMR (600 MHz;  $\text{CDCl}_3$ , 298 K)  $\delta$  5.22-5.11 (m,  $\text{C(O)CH(CH}_3\text{)O}$  2H), 4.13 (br s,  $\text{CH}_2\text{CH}_2\text{OC(O)CH(CH}_3\text{)}$  1H), 4.06 (t,  $\text{CH}_2\text{CH}_2\text{OC(O)CH}_2\text{CH}_2$ , 1H), 2.39 (br s,  $\text{CH(CH}_3\text{)OC(O)CH}_2\text{CH}_2\text{CH}_2$ , 1H), 2.31 (t,  $\text{CH}_2\text{CH}_2\text{OC(O)CH}_2\text{CH}_2\text{CH}_2$ , 1H), 1.67-1.36 (br m,  $\text{CH(CH}_3\text{)}$ ,  $\text{C(O)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$  12H).

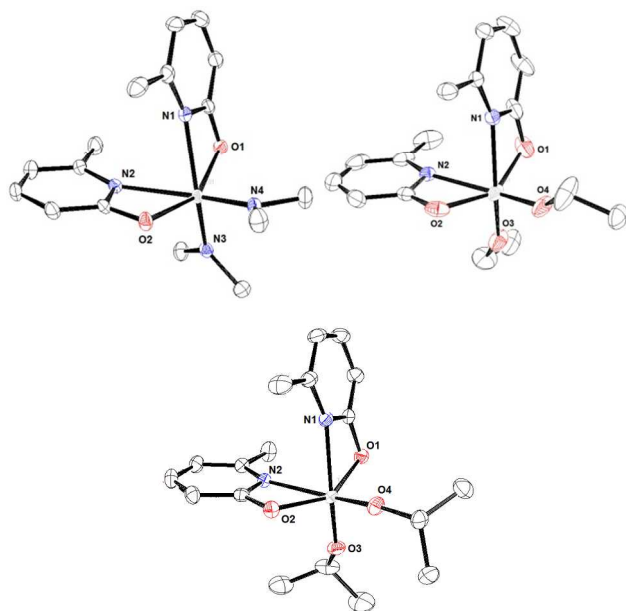
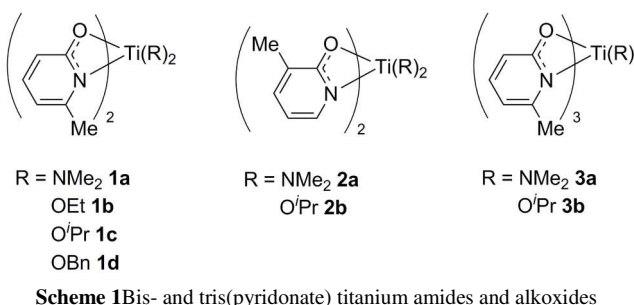
**General procedure for the block copolymerization of LA and CL.** In a nitrogen filled glovebox, a Kontes®-valve reaction tube was charged with a stirrer bar and the appropriate quantity of catalyst was added from a standard solution in toluene. The solvent was then removed in *vacuo*. Block copolymerizations began with the addition of  $\epsilon$ -CL (clear, colorless liquid, 300 equivalents,  $0.396 \text{ g}$ ,  $114.14 \text{ g}\cdot\text{mol}^{-1}$ ). This was followed by heating at  $100 \text{ }^\circ\text{C}$  using a preheated oil bath for 16 h. The reaction tube was then returned to the glovebox and *rac*-LA (clear, colorless solid, 300 equivalents,  $0.500 \text{ g}$ ,  $144.13 \text{ g}\cdot\text{mol}^{-1}$ ) was added, followed by heating at  $130 \text{ }^\circ\text{C}$  for 24 h. The reaction was then worked-up as with the above polymerizations to obtain the isolated polymer (off-white, solid).

**Poly(lactide-co-caprolactone) PLA-co-PCL** (see SI)  $^1\text{H}$  NMR (300 MHz;  $\text{CDCl}_3$ )  $\delta$  5.22-5.14 (m,  $\text{C(O)CH(CH}_3\text{)O}$  2H), 4.06 (t,  $\text{CH}_2\text{CH}_2\text{OC(O)CH}_2\text{CH}_2\text{CH}_2$ , 2H), 2.32 (br t,  $\text{CH}_2\text{CH}_2\text{OC(O)CH}_2\text{CH}_2\text{CH}_2$ , 2H), 1.67-1.52 (br m,  $\text{CH(CH}_3\text{)}$ ,  $\text{C(O)CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}$  12H).

## Results and Discussion

### Synthesis of Initiators

Titanium-pyridonate complexes (Scheme 1) were formed in high yield at room temperature by combining the homoleptic starting material with the desired proligand. Transformation of the dimethylamido species (for example **1a**, **2a** and **3a**) into the related alkoxide is readily achieved within minutes at room temperature by the addition of a stoichiometric amount of alcohol.<sup>37</sup> A range of sterically varied alkoxides can be used without adversely affecting the yield (compare **1b**, **1c** and **1d**). It was of interest to compare the difference in reactivity of **1a** through **1d** to investigate whether a change in the reactive ligand systematically influences polymerization. Variable substitution patterns on the pyridonate ring at the 3- and 6- position were also tolerated (compare **1a**, **2a** and **1c**, **2b**). Crystals of **1a**, **1b** and **1c** were grown by slow evaporation of a hexane solution. Crystals of **2a** could be grown by slow evaporation of a super-saturated benzene solution.

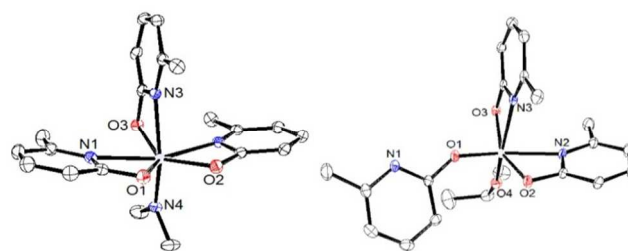


**Figure 2** ORTEP representation of the solid state molecular structures of **1a** (top-left), **1b** (top-right) and **1c** (bottom-center); thermal ellipsoids set at 50%. **1a** selected bond lengths (Å) Ti-O1 2.035(1), Ti-O2 2.016(2), Ti-N1 2.284(2), Ti-N2 2.267(3), Ti-N3 1.884(2), Ti-N4 1.910(3) and angles (°) N1-Ti-O1 61.58(8), N2-Ti-O2 62.11(8). **1b** selected bond lengths (Å) Ti-O1 2.012(3), Ti-O2 2.006(3), Ti-N1 2.234(3), Ti-N2 2.214(3), Ti-O3 1.784(3), Ti-O4 1.794(3) and angles (°) N1-Ti-O1 62.74(11), N2-Ti-O2 62.70(10). **1c** selected bond lengths (Å) Ti-O1 2.003(1), Ti-O2 1.986(1), Ti-N1 2.219(1), Ti-N2 2.250(2), Ti-O3 1.785(1), Ti-O4 1.766(1) and angles (°) N1-Ti-O1 62.72(5), N2-Ti-O2 62.51(5).

Bis(ligated) complexes are typically anticipated to furnish

systems that initiate twice to yield two growing polymer chains per metal. In an effort to probe the steric environment about the metal center, the preparation of a tris-pyridonate complex was pursued, as this system would be expected to afford only one growing polymer chain per metal. These targeted complexes could be readily prepared by simply changing the ligand stoichiometry and it was found that both the mono(dimethylamido), **3a**, and mono(isopropoxide) species, **3b**, can be synthesized in high yield. Analysis of the solid-state molecular structure reveals that **3a** maintains an unusual 7-coordinate ligation mode, displaying a distorted pseudo tetrahedral geometry around the metal center (Figure 3), with each N,O-chelate being assigned a coordination number of 1. Similar to the bis-coordinated analogues, **1-2**, an unsymmetrical binding of the N,O chelate is observed. It is also interesting to note that all three pyridonate ligands are relatively symmetrical to one another, with only a slight lengthening of the N3-Ti and O3-Ti bond lengths and marginal widening of the N3-Ti-O3 bond angle.

In the isopropoxide complex **3b**, one of the pyridonates is  $\kappa^1$  in the solid state. The introduction of an alkoxide ligand and a concomitant increase in  $\pi$ -donation to the metal center does result in a slight lengthening of the *trans* Ti-N3 bond (compare **3a** Ti-N3 2.169(2) to **3b** Ti-N3 2.229(1)). However, analysis of these complexes by <sup>1</sup>H NMR spectroscopy shows primarily one set of resonances that can be assigned to the pyridonate ring. Therefore, fluxional behaviour is occurring at a rate faster than the NMR timescale.



**Figure 3** ORTEP representation of the crystal structures of complexes **3a** (left) and **3b** (right); thermal ellipsoids set at 50%. Selected bond lengths of **3a**: Ti-N1 2.267(1), Ti-N2 2.270(1), Ti-N3 2.169(2), Ti-N4 1.873(2), Ti-O1 2.018(2), Ti-O2 2.009(2), Ti-O3 2.059(2); bond angles N1-Ti-O1 61.17(6), N2-Ti-O2 61.13(6), N3-Ti-O3 62.56(6). Selected bond lengths of **3b**: Ti-N2 2.200(2), Ti-N3 2.229(1), Ti-O1 1.846(1), Ti-O2 2.001(2), Ti-O3 1.983(1), Ti-O4 1.752(1); bond angles N2-Ti-O2 62.34(5), N3-Ti-O3 62.98(5).

Presumably, all three pyridonate ligands show hemilability and fluctuate between these  $\kappa^2$ - $\kappa^1$  coordination modes in solution.

With this family of titanium complexes in hand, exploration of initiating ligand, pyridonate substituent effects and number of growing polymer chains per metal can be explored. These variable effects provide insight into how lactone ROP is proceeding with this new class of complexes.

#### Homopolymerization of *rac*-Lactide and $\epsilon$ -Caprolactone

Initially, different reaction conditions were screened for the synthesis of PLA. However, it soon became clear that polymerization is favoured in the melt phase. Solution phase reactions (for example 3.45 M solutions of refluxing THF or

toluene) gave greatly reduced yields and with it far inferior  $M_n$  values. Therefore, polymerizations for comparison purposes were carried out at 130 °C for 24 h using a monomer to initiator ratio of 300 to 1.

**Table 1.** Homopolymerization of *rac*-lactide with complexes **1a-3b**

Entry	Catalyst	Yield (%) <sup>a</sup>	$M_n$ (g·mol <sup>-1</sup> ) <sup>b</sup>	$M_n$ theor. (g·mol <sup>-1</sup> ) <sup>c</sup>	$\bar{D}^b$	$P_m^d$
1	<b>1a</b>	91	17,500	19,670	1.22	0.49
2	<b>1b</b>	91	21,210	19,670	1.28	0.51
3	<b>1c</b>	88	13,800	19,030	1.17	0.49
5	<b>1d</b>	93	14,380	20,110	1.19	0.49
6	<b>2a</b>	92	23,070	19,890	1.44	0.49
7	<b>2b</b>	90	14,120	19,460	1.21	0.46
8	<b>3a</b>	96	15,260	41,510 <sup>e</sup>	1.18	0.51
9	<b>3b</b>	82	16,410	35,460 <sup>e</sup>	1.16	0.50

Reaction conditions: 130 °C, 24 h, [LA]/[Ti] = 300, 0.5 g. <sup>a</sup>Isolated yield.

<sup>b</sup>Determined by GPC. <sup>c</sup> $M_n$ theor. = ([LA]/2[Ti]·%Yield·144.13 g·mol<sup>-1</sup>)

<sup>d</sup><sup>1</sup>H {<sup>1</sup>H} NMR spectrum. <sup>e</sup> $M_n$ theor. = ([LA]/[Ti]·%Yield·144.13 g·mol<sup>-1</sup>).

Table entries are averaged values for experiments performed in duplicate, with the experimental molecular weights determined within +/- 10%. Comparison of polymer molecular weights found for initiators **1a-3b** do not vary significantly. Comparing initiators **1a** through to **1d**, molecular weights generally trend with theoretical molecular weights calculated with the assumption that each initiator forms two polymer chains. Control, assessed by the dispersity ( $\bar{D}$ ) of molecular weights obtained, is moderate, ranging from 1.16 to 1.44. Notably, in contrast to previous reports,<sup>21</sup> an amido initiating ligand compares favourably with an alkoxide initiating ligand (compare **1a** and **1c** as well as **2a** and **2b**). No meaningful difference is observed in comparison between pyridonates with methyl substitution at the 3- vs. the 6-position (**1a**, **1c** vs. **2a**, **2b**), suggesting the relative position of the methyl group does not dramatically impact the steric environment about the metal center. As all  $P_m$  (probability of meso enchainment) values are close to 0.50, these initiators demonstrate no stereo-preference when polymerizing racemic lactide.

Interestingly, the experimental  $M_n$  values for the tris-ligated complexes do not provide a good match to the theoretical value, presuming that only one polymer chain can propagate per metal center. <sup>1</sup>H NMR analysis of the isolated polymers confirms only dimethyl amino (**3a**) or isopropylalkoxide (**3b**) end-groups; no aryl signals could be observed in the NMR spectrum. This therefore rules out initiation by the pyridonate ligand via a coordination-insertion mechanism. This could arise from transesterification of the PLA product.

**Table 2.** Homopolymerization of  $\epsilon$ -caprolactone with complexes **1a-3b**

Entry	Catalyst	Yield (%) <sup>a</sup>	$M_n$ (g·mol <sup>-1</sup> ) <sup>b</sup>	$M_n$ theor. (g·mol <sup>-1</sup> ) <sup>c</sup>	$\bar{D}^b$
1	<b>1a</b>	89	20,670	15,240	1.32
2	<b>1b</b>	85	31,785	14,449	1.34
3	<b>1c</b>	98	39,400	16,780	1.29
4	<b>1d</b>	92	19,720	15,750	1.22
5	<b>2a</b>	92	22,470	15,750	1.35
6	<b>2b</b>	89	23,570	15,237	1.32
7 <sup>d</sup>	<b>3a</b>	79	30,600	27,050	1.25
8 <sup>d</sup>	<b>3b</b>	84	33,500	28,760	1.16

<sup>a</sup> Reaction conditions: 100 °C, 16 h, [CL]/[Ti] = 300, 0.396 g. <sup>b</sup>Isolated yield. <sup>c</sup>Determined by GPC. <sup>d</sup> $M_n$ theor. = ([CL]/2[Ti]·%Yield·114.14 g·mol<sup>-1</sup>) <sup>e</sup> $M_n$ theor. = ([CL]/[Ti]·%Yield·114.14 g·mol<sup>-1</sup>).

Proceeding to explore the use of our metal initiators in the synthesis of PCL, we continued to use solvent-free reaction conditions (Table 2). The lowered reaction times and temperatures to reach completion suggest these initiators are more reactive toward  $\epsilon$ -caprolactone. This is corroborated by the ring strain of the respective monomers (-28.8 kJ·mol<sup>-1</sup> vs. -22.9 kJ·mol<sup>-1</sup> for L,L-lactide),<sup>38</sup> which is attributed to be the driving force of polymerization. In the case of the bis(pyridonate) complexes the obtained molecular weights are in excess of the molecular weight proposed for a bis-initiating and propagating complex. This can be rationalized by two possibilities: 1) some initiators are operating as a mono-initiation and propagation site with only one growing polymer chain per metal center, or 2) not all of the initiators are active, either by undesired deactivation by side reactions or by denied access to the monomer due to limited diffusion as the viscosity of the reaction mixture increases. Either possibility will result in molecular weights in excess of theoretical molecular weights calculated based upon two growing polymer chains per metal center.

Once again, end-group analysis shows only alkoxide or dimethylamido chain ends. As in PLA synthesis, there is no evidence to suggest incorporation of pyridonate groups into the chain ends, as evidenced by the lack of aromatic signals in the <sup>1</sup>H NMR spectrum.

While the polymer characterization metrics of the obtained materials vary slightly with the initiator chosen, overall the differences suggest that varying the nature of the pyridonate substitution or reactive ligand has only slight effects on the resulting polymer properties. Although  $\epsilon$ -caprolactone can be considered more reactive based on milder experimental conditions, molecular weight data does not suggest that initiation is controlled for the bis-pyridonate complexes **1-2**. Meanwhile, the generally lower experimental molecular weights obtained in the polymerization of *rac*-lactide relative to theoretically predicted values suggest it may be more prone to transesterification reactions, as has been previously observed in co-polymerization investigations.<sup>15</sup> These comparative reactivities can be further contrasted in attempts to form copolymers.

### Random Copolymerization of *rac*-Lactide and $\epsilon$ -Caprolactone

Given the capacity of the initiators to form homopolymers in high yield, their ability to form a random copolymer by simultaneously reacting them with *rac*-lactide and  $\epsilon$ -caprolactone was attempted. Previously, it was reported by our group that the

titanium pyridonates were able to form random copolymers of poly(lactide-*co*-caprolactone) with equal incorporation of both monomers.<sup>15</sup> Equal incorporation of both monomers is an important synthetic challenge because of the inherent reactivity differences between the monomers.<sup>12</sup> For example, other reported examples of titanium-based random copolymer formation show a deficit of  $\epsilon$ -caprolactone incorporation when copolymer synthesis is attempted.<sup>12-14</sup> As these pyridonates are a rare class of titanium initiator capable of realizing the synthesis of random copolymers, further investigations of pyridonate initiator derivatives were explored with the expanded library of complexes.

**Table 3.** CL/LA random copolymerization with complexes **1a-3b**

Entry	Cat.	Yield (%) <sup>a</sup>	CL/LA <sup>b</sup>	$L_{CL}/L_{LL}$ <sup>c</sup>	Hetero Diads (%) <sup>d</sup>	$M_n$ (g·mol <sup>-1</sup> ) <sup>e</sup>	$M_n$ theo (g·mol <sup>-1</sup> ) <sup>f</sup>	$\bar{D}^g$
1	<b>1a</b>	72	50/50	1.9/3.4	48	20,660	28,930	1.37
2	<b>1b</b>	81	51/49	2.0/4.9	49	54,065	31,154	1.79
3	<b>1c</b>	82	45/55	1.8/3.4	51	18,750	33,390	1.41
4	<b>1d</b>	82	49/51	1.9/6.8	44	56,170	31,734	1.64
5	<b>2a</b>	70	44/56	1.7/5.2	53	27,920	26,379	1.39
6	<b>2b</b>	83	52/48	1.9/2.9	46	19,070	33,190	1.29
7 <sup>g</sup>	<b>3a</b>	75	48/52	1.9/3.0	44	19,370	58,050	1.35
8 <sup>g</sup>	<b>3b</b>	56	23/77	-	73	18,610	43,344	1.32

Reaction Conditions: 0.396 g CL, 0.5 g LA, 130 °C, 24 h. Total [monomers]/[Ti] = 600. <sup>a</sup>Isolated yield. <sup>b</sup>Determined by <sup>1</sup>H NMR spectroscopy. <sup>c</sup>Determined by <sup>13</sup>C {<sup>1</sup>H} NMR spectroscopy. <sup>d</sup>Ratio of CL homo vs. hetero signals in <sup>1</sup>H NMR spectrum. <sup>e</sup>Determined by GPC. <sup>f</sup> $M_n$  theo. =  $[(CL)/2[Ti] \cdot \%_{conv}CL \cdot 114.14 \text{ g} \cdot \text{mol}^{-1}] + [(LA)/2[Ti] \cdot \%_{conv}LA \cdot MW_{LA}] \cdot \%Yield$  <sup>g</sup> $M_n$  theo. =  $[(CL)/[Ti] \cdot \%_{conv}CL \cdot 114.14 \text{ g} \cdot \text{mol}^{-1}] + [(LA)/[Ti] \cdot \%_{conv}LA \cdot MW_{LA}] \cdot \%Yield$

With the exception of initiator **3b** (entry 8), all initiators are able to produce a copolymer in reasonable yield with near equal incorporation of both monomers. The ratio of the monomers was determined by taking the ratio of the signals assigned to the methine protons of poly(lactic acid) ( $\delta$  5.16 ppm) to the methylene protons of poly( $\epsilon$ -caprolactone) ( $\delta$  4.20–4.00 ppm) in the <sup>1</sup>H NMR spectrum. Initiator **3b** shows a reactivity profile more typical of Ti initiators; the preferential incorporation of lactide over  $\epsilon$ -caprolactone.<sup>12-14</sup> Inspection of the resonance assigned to the poly( $\epsilon$ -caprolactone) methylene protons shows two distinct peaks ( $\delta$  4.16 and 4.06 ppm) which differentiate CL-LA heterojunctions (lying slightly downfield due to greater deshielding by the adjacent poly(lactic acid) segment) and CL-CL homojunctions (4.06 ppm). With the exception of entry 8, all obtained polymers give close to the desired 50% heterojunctions for a random copolymer. Average sequence lengths ( $L_{CL}/L_{LL}$ ) of the respective poly( $\epsilon$ -caprolactone) and poly(lactic acid) segments were calculated using the carbonyl region ( $\delta$  174–169 ppm) in the <sup>13</sup>C {<sup>1</sup>H} NMR spectrum. Calculated values show close to two for poly( $\epsilon$ -caprolactone) segments while poly(lactic acid) units were slightly longer, with average lengths between 3.5 and 5. According to assignments made by Bero and Kasperczyk,<sup>39</sup> the signal at  $\delta$  171.1 ppm can be assigned to a 'CLC' sequence (where C and L refer to caprolactone and lactide respectively). Since the lactide monomer is an LL dimer (see Figure 1), a sequence with a single lactide ester resonance can only originate from a chain transfer event such as transesterification. A clear signal at 171 ppm is evident in the spectra of the random copolymers prepared here. Furthermore

these random copolymers have been reported to arise from transesterification by monitoring the consumption of each monomer and the formation of homo- and heterodiads as a function of time.<sup>15</sup> Notably, such reaction monitoring showed that lactide was incorporated into the polymer chain preferentially at the outset of co-polymerization, however, extensive transesterification upon  $\epsilon$ -caprolactone incorporation was observed by NMR spectroscopy. Specifically, there was a sharp increase in the number of CL-LA heterojunctions triggered by CL incorporation rather than the expected CL-CL homojunction formation.<sup>40</sup> While the mechanism of copolymerization and transesterification is poorly understood in these systems, these transesterification processes have been shown to result in the randomization of the polymer backbone.<sup>3,15</sup>

Entries 2 and 4 have noticeably large molecular weight, this indicates that initiation with the ethoxide and benzyl alkoxide reactive ligands may be sluggish relative to the dimethylamido or isopropoxide ligands in random copolymer synthesis. As described in PCL synthesis, poor initiation is believed to result in larger molecular weights when using the bis-pyridonate initiators. With the exception of these entries, the obtained molecular weights are less than the predicted theoretical values. This suggests transesterification side reactions are occurring, producing shorter chains due to chain scission events while randomizing the monomers along the polymer backbone. These initiators are a rare example of a titanium complex able to afford equal monomer incorporation given an equimolar monomer feed. While these results show random copolymers can be generated, the ability to further understand transesterification reactions in these titanium initiated polymerizations is highly desired.

## Block Copolymerization of *rac*-Lactide and $\epsilon$ -Caprolactone

Beyond the ability to form random copolymers, the initiators' ability to form block copolymers was explored. Block copolymers are comprised of two subunits, in this case a segment of poly(lactic acid) with ideally a single heterojunction to a block or segment of poly( $\epsilon$ -caprolactone). The attempted synthesis of these copolymers with titanium pyridonate initiators was performed using sequential addition of the monomers, thereby forming polymer chains of one monomer followed by addition and polymerization of the second monomer.

In the case of these initiators, it was found that attempts to polymerize *rac*-lactide first into poly(lactic acid) followed by addition of  $\epsilon$ -caprolactone resulted in a polymer that features little to no incorporation of  $\epsilon$ -caprolactone. However, when the order was reversed and poly( $\epsilon$ -caprolactone) was preformed, followed by addition of *rac*-lactide, the desired copolymer was obtained.



**Table 4.** CL-LA block copolymerization with complexes **1a-3b**

Entry	Catalyst	Yield (%) <sup>a</sup>	CL/LA <sup>b</sup>	$M_n$ (g·mol <sup>-1</sup> ) <sup>c</sup>	$M_n$ theor. (g·mol <sup>-1</sup> ) <sup>d</sup>	$\bar{D}^e$
1	<b>1a</b>	80	55/45	21,450	31,382	1.41
2	<b>1b</b>	81	55/45	61,660	31,774	1.25
3	<b>1c</b>	86	51/49	23,770	33,230	1.28
4	<b>1d</b>	82	55/45	40,000	32,087	1.24
5	<b>2a</b>	83	56/44	26,185	32,559	1.37
6	<b>2b</b>	77	56/44	20,720	29,430	1.31
7 <sup>f</sup>	<b>3a</b>	68	57/43	46,280	52,632	1.53
8 <sup>f</sup>	<b>3b</b>	66	59/41	44,440	51,858	1.37

Reaction Conditions: 0.396 g CL, 100 °C, 16 h then 0.5 g LA, 130 °C, 24 h. Total [monomers]/[Ti] = 600. <sup>a</sup>Isolated yield. <sup>b</sup>Determined by <sup>1</sup>H NMR spectroscopy. <sup>c</sup>Determined by GPC. <sup>d</sup> $M_n$ theor. =  $[(\text{CL})/2[\text{Ti}] \cdot$

$\%_{\text{conv}}\text{CL} \cdot 114.14 \text{ g} \cdot \text{mol}^{-1}) + ([\text{LA}]/2[\text{Ti}] \cdot \%_{\text{conv}}\text{LA} \cdot 144.13 \text{ g} \cdot \text{mol}^{-1})] \cdot$   
 $\% \text{Yield} \cdot M_n \text{theor.} = [([\text{CL}]/[\text{Ti}] \cdot \%_{\text{conv}}\text{CL} \cdot 114.14 \text{ g} \cdot \text{mol}^{-1}) + ([\text{LA}]/[\text{Ti}] \cdot$   
 $\%_{\text{conv}}\text{LA} \cdot 144.13 \text{ g} \cdot \text{mol}^{-1})] \cdot \% \text{Yield}$

While the yields obtained were generally lower than those obtained for the homopolymerizations, block copolymers were obtained in reasonably good yields with moderate levels of control. Inspection of the downfield poly( $\epsilon$ -caprolactone) methylene signal in the <sup>1</sup>H NMR spectrum shows a triplet at  $\delta$  4.06 ppm with no detectable resonance at  $\delta$  4.13 ppm that could be assigned to a CL-LA heterojunction (as in the random copolymers). This indicates that segments of ring-opened  $\epsilon$ -caprolactone appear to be homocoupled to one another, suggesting the desired block segment of poly( $\epsilon$ -caprolactone) is present in the obtained polymer and there has been little to no transesterification into this block. The ratio of the monomers incorporated was determined by comparison of this signal to the methine protons of poly(lactic acid) at  $\delta$  5.16 ppm and in all cases showed only a slight over incorporation of poly( $\epsilon$ -caprolactone). For the polymers formed with bis(pyridonate) initiators, molecular weights are lower than theoretically predicted, with the exception of the complexes with the ethoxide and benzoxide reactive ligands (entries 2 and 4). It is speculated that these reactive ligands may arise in sluggish rates of initiation compared to the dimethylamido or isopropoxide ligands, once again resulting in larger molecular weights than predicted. In the case of the tris(pyridonate) initiators which are expected to mono-propagate, the obtained molecular weights agree well with predicted theoretical values, albeit with diminished yields. Interestingly, the results obtained here suggest transesterification between the blocks is not significant. If chain transfer was occurring to a large extent, we would expect to observe CL-LA heterojunctions in the <sup>1</sup>H NMR spectrum of these polymers. Furthermore, significantly diminished molecular weight was not observed to the same extent as was observed in random copolymer synthesis. These differences highlight the effect of simultaneous vs sequential addition in attempts to form random or block copolymers respectively.

A critical mechanistic question that has surrounded polymerizations with the bis-pyridonate complexes is whether they are able to initiate and propagate two polymer chains per metal center. Since the initial disclosure of these bis(pyridonate) complexes, it was hypothesized that the synthesis of the tris(pyridonate) complexes would provide an insightful comparison in reactivity. The results explored here generally suggest mono-initiation and propagation with the tris(pyridonate)

initiators; however, they do not differ as dramatically as anticipated from the results obtained with the bis(pyridonate) initiators. While the number of propagating chains cannot be inferred from molecular weight data in the case of poly(lactic acid) synthesis, the lower than predicted experimental molecular weights suggest that transesterification plays a significant role when attempting to polymerize this monomer.

## Conclusions

Dimethylamido and alkoxide complexes of titanium bearing pyridonate ligands have demonstrated their utility in the ring-opening polymerization of *rac*-lactide and  $\epsilon$ -caprolactone to afford homopolymers as well as block and random copolymers. While not yet possessing the high activity and control demonstrated by leading initiators,<sup>41</sup> these complexes are competitive with other reported titanium initiators.<sup>12, 16, 18, 20</sup> Notably, the ability to form random copolymers with close to equal monomer incorporation makes these complexes distinguished amongst titanium complexes. Furthermore, the ability to form block copolymers comprised of equimolar monomer incorporation by using sequential  $\epsilon$ -caprolactone followed by lactide monomer addition highlights the versatility of these initiators. While the variations of initiator design explored herein do not dramatically affect the resulting polymer properties, the overall scope of reactivity of these Ti pyridonate complexes shows that they provide a favourable steric and electronic environment about the metal center for unique trends in ROP.

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## Notes and references

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